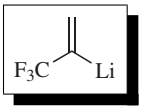
1-(Trifluoromethyl)vinyllithium



[14856-85-0] $C_3H_2F_3Li$ (MW 101.98)

InChI = 1/C3H2F3.Li/c1-2-3(4,5)6;/h1H2;/rC3H2F3Li/c1-2(7)3(4,5)6/h1H2

InChIKey = YDBNXCHLLXTABG-DUEXXTGJAC

(reagent used as a versatile vinylation component)

Physical Data: thermally unstable; decomposes quickly at temperatures above −78 °C.

Solubility: soluble in diethyl ether, pentane, and THF.

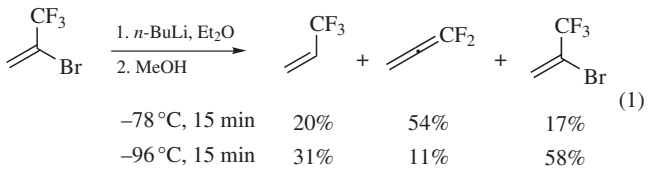
Form Supplied in: not available commercially.

Preparative Method: prepared from the reaction of commercially available 2-bromo-3,3,3-trifluoropropene with *n*-, *sec*-, or *tert*-butyllithium in diethyl ether at −100 to −110 °C.[1]

Handling, Storage, and Precautions: prepared and transferred at low temperature (≤ −100 °C) under inert atmosphere (Ar); air and moisture sensitive; handle in fume hood.

Vinylations. 1-(Trifluoromethyl)vinyllithium is a valuable reagent that provides a variety of compounds bearing a (trifluoromethyl)vinyl moiety. The moiety has much synthetic potential due to its reactive double bond toward nucleophiles and its allylic fluorine atoms that act as leaving groups.[2,3] 2-(Trifluoromethyl) allylic alcohols have been prepared by the treatment of aldehydes and ketones with highly reactive 1-(trifluoromethyl)vinyllithium derived from 2-bromo-3,3,3-trifluoropropene in situ at low temperature.[4,5] However, this approach to prepare nonconjugated (trifluoromethyl)vinyl compounds has several drawbacks such as incomplete lithium-halogen exchange and the generation of a considerable amount of 1,1-difluoroallene as a by-product.[6]

The reaction of 2-bromo-3,3,3-trifluoropropene with *n*-butyllithium to produce 1-(trifluoromethyl)vinyllithium reagent has been reexamined under different conditions by Ichikawa et al.[6] It shows that 3,3,3-trifluoropropene and 1,1-difluoroallene, generated by the decomposition of 1-(trifluoromethyl)vinyllithium species via elimination of lithium fluoride, can be obtained in 20 and 54% yields, respectively, along with 17% of recovered starting material (eq 1). In addition, the decomposition of the thermally unstable lithium species to 1,1-difluoroallene occurs even at −96 °C and a significant amount of the starting material, 2-bromo-3,3,3-trifluoropropene, remains at this temperature. Studies have shown that 1,1-difluoroallene can be delivered in 72% yield together with the quantitative production of lithium fluoride when 1-(trifluoromethyl)vinyllithium is prepared at −90 °C and warmed to room temperature.[4] Different solvent systems have also been studied in an attempt to prepare 1-(trifluoromethyl)vinyllithium.

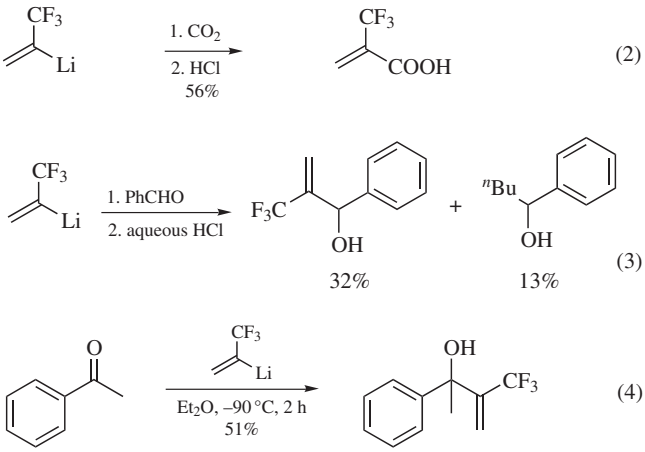


–78 °C, 15 min	20%	54%	17%
–96 °C, 15 min	31%	11%	58%

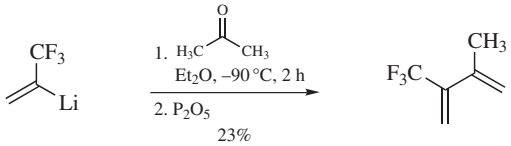
(1)

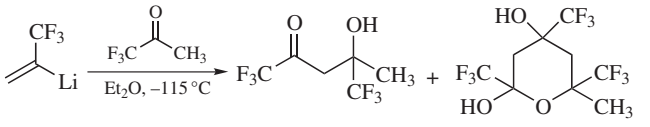
Lithium-bromide exchange does not occur in hexane solution, and in tetrahydrofuran solution, extensive degradation takes place and no useful products are found.

Therefore, there are two different techniques developed for the preparation of 1-(trifluoromethyl)vinyllithium and its reactions with carbonyl compounds.[4] When the carbonyl compound is a gas such as carbon dioxide, 1-(trifluoromethyl)vinyllithium is prepared at −110 °C and the gas is passed into the reaction mixture. 2-Trifluoromethylacrylic acid can be obtained in 56% yield though this process (eq 2). When the carbonyl compound is a liquid, the alternate aliquots of *n*-butyllithium and carbonyl compound are added to 2-bromo-3,3,3-trifluoropropene solution. With this method, 1-(trifluoromethyl)vinyllithium is immediately formed reacting with carbonyl compounds at around −100 °C. α-(Trifluoroisopropenyl)benzyl alcohol and methylphenyl(trifluoroisopropenyl)carbinol have been synthesized in 32% (eq 3) and 51% (eq 4) yield, respectively, via this procedure.[4]



It has been shown that the reaction of 1-(trifluoromethyl)vinyllithium with a carbonyl compound, possessing hydrogen atoms at α-carbon position, affords a general route to substituted butadiene as a dehydration product in high yields by heating with phosphorus pentoxide.[4] For example, treatment of acetone with 1-(trifluoromethyl)vinyllithium reagent affords the corresponding carbinol in 46% yield followed by dehydration with phosphorus pentoxide to furnish 2-methyl-3-(trifluoromethyl)buta-1,3-diene in 49% yield (eq 5). However, the reaction with trifluoroacetone is abnormal. The expected carbinol 1,1,1-trifluoro-2-methyl-3-(trifluoromethyl)but-3-en-2-ol has not been obtained after the reaction of trifluoroacetone with 1-(trifluoromethyl)vinyllithium under several different conditions studied.[4] Instead, mixtures of 1,1,1,5,5,5-hexafluoro-4-hydroxy-4-methylpentan-2-one and a pyran derivative are found due to the cyclization reaction of trifluoroacetone (eq 6).[7] This indicates that 1-(trifluoromethyl)vinyllithium preferentially abstracts a proton from trifluoroacetone rather than attacking the carbonyl function.



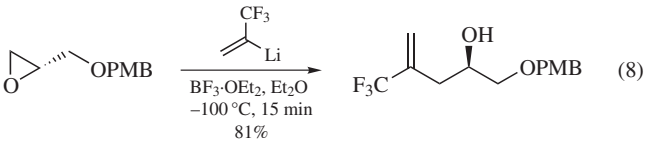


(6)

The formation of a (trifluoromethyl)vinyl derivative of silicon has been investigated by the reaction between 1-(trifluoromethyl) vinyllithium and triethylchlorosiliane (eq 7).[4] However, the only product obtained is triethylfluorosilane in a low yield. It shows that possibly fluorine migrates to the silicon atom with elimination of difluoroallene after the initial formation of triethyl(3,3,3-trifluoroprop-1-en-2-yl)silane.

(7)

Oxirane and Oxetane Ring-opening Reactions. The reaction of several oxiranes with 1-(trifluoromethyl)vinyllithium in the presence of a stoichiometric amount of $BF_3{\cdot}OEt_2$ to obtain expected 3-(trifluoromethyl)homoallylic alcohols has been examined by Ichikawa et al.[6,8] 1-(Trifluoromethyl)vinyllithium can be generated by the addition of *n*-butyllithium to the mixture of 2-bromo-3,3,3-trifluoropropene and $BF_3{\cdot}OEt_2$in diethyl ether at −100 °C followed by treatment with an oxirane to furnish the corresponding homoallylic alcohol in high yields.[9] For example, an optically active epoxide can be transformed into a partially protected diol in 81% yield without racemization (eq 8).[10] Treatment of styrene oxide with 1-(trifluoromethyl)vinyllithium affords a mixture of regioisomers (eq 9). Studies have revealed that the ratio of regioisomers can be modified by exploiting different alkyllithiums and by changing the addition order of the reagents. For instance, when the reagents are added in the following order: 2-bromo-3,3,3-trifluoropropene, $BF_3{\cdot}OEt_2$, styrene oxide, and *n*-butyllithium, the ratio of two isomers can be changed from 1:4 to 2:1 (eq 9). A 2,3-disubstituted oxirane, cyclohexene oxide, can also be applied in this reaction, leading to the expected cyclohexanol in 40% yield (eq 10).[6]



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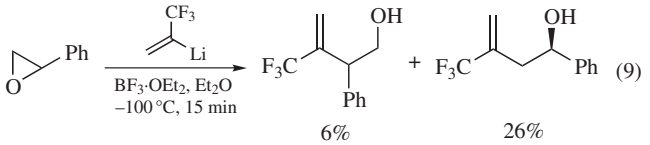

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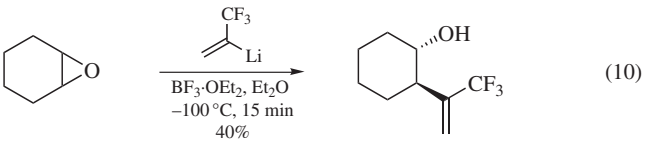
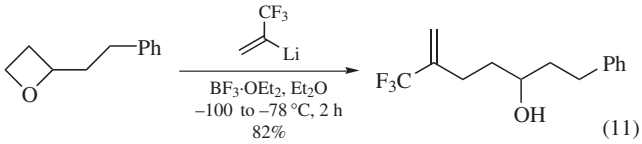


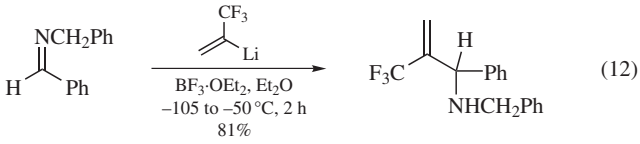
(10)

This method can be utilized in another strained cyclic ether system, oxetane, to provide alkyl alcohols bearing a 1-(trifluoromethyl)vinyl unit.[6] Treatment of 2-phenethyloxetane with 1-(trifluoromethyl)vinyllithium produces 1-phenyl-6-(trifluoromethyl) hept-6-en-3-ol in 30% yield under the same conditions as above (−100 °C and 15 min). Nevertheless, the reaction can be optimized to give a higher yield with a longer reaction time and 3 equiv of the lithium species (eq 11).[11]



(11)

Formation of *N*-Allylamines and *N*-Allylamides. Allylamines have been employed as very useful building blocks for the synthesis of *N*-heterocycles. The reaction of 1-(trifluoromethyl) vinyllithium with imines for the preparation of 2-(trifluoromethyl) allylamines has been reported.[1,12] The reaction of *N*-benzylimine can be promoted by $BF_3{\cdot}OEt_2$ to furnish the desired amine in 81% yield (eq 12). Under similar conditions, *N*-benzoyl and *N*-tosylimine have been applied as reactive electrophiles to afford the corresponding *N*-allylamides in 97 and 90% yield, respectively (eqs 13 and 14).



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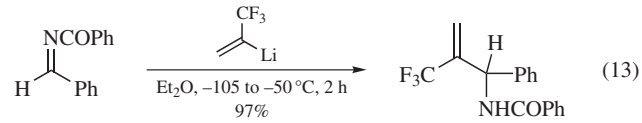

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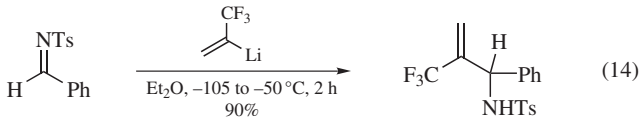

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